

# AAAAI Ask the Expert Feed

## Lactose in asthma inhalers

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Some inhaled asthma medications (Pulmicort, Advair) contain small amounts of lactose and possibly small amounts of milk proteins. Is there a real danger here for milk-allergic patients, or does it seem to be more of a theoretical concern? Thank you very much.  
Thank you for your recent inquiry.



The answer to a very similar inquiry was posted on the Ask the Expert website on June 15, 2008. There has been no update in the status of this subject since that answer was posted.

For your convenience, therefore, I have copied below the similar inquiry and the response from both me and from Dr. Scott Sicherer.

Thank you again for your inquiry and we hope this response is helpful to you.

Are Lactose Containing Inhalers Safe to Use in Milk Allergic Asthmatic Children?

6/15/2008

Question:

Milk and Milk protein allergy - beef protein allergy also.

I have a 9 year old with Class III milk allergy ( as a whole with the Whey component still staying at IV)

And Beef class III- which was an increase

I am a pharmacist whom recently noticed Advair Discus has milk protein in it ( just after it was prescribed for said child )

But I also know that he had BEEF LUNG SURFACTANT /BERACTANT (survanta)

At less than 12 hours old when placed on a ventilator at 31 weeks gestation.

He has no other food allergies and no other significant allergies ( dog dander - minor allergist suggested him staying around the babysitters dog at the time )

Could there be a link?

Answer:

I am not quite sure of the intent of the question that you ask, which was "could there be a link?" I am not sure whether you mean a link between these food allergies and the use of the Advair, or a link between his asthma and the use of Advair.

Although I am not quite sure about the exact nature of your question - that is, what the question refers to - I am still going to take this opportunity to give you some information regarding this issue.

Our web site has received other inquiries regarding this same subject, and I am copying below a response from both me and Dr. Scott Sicherer (who is an internationally known expert in food allergy) about the topic of whether or not it is safe for a milk allergic child to use an asthma inhaler containing lactose.

In addition, I am sending you further information from another web site which offers information also dealing with this issue.

As you can see from these responses, a number of different asthma inhalers contain lactose. You can also see that the vast majority of children who are allergic to milk can tolerate these inhalers without difficulty. In addition, in most instances, to cause asthma, it takes a far larger amount of milk protein than that which is a contaminant in these lactose containing inhalers. However, there are case reports (a reference is noted in my original response seen below) of children having trouble with their asthma when they use these inhalers.

The only real way to know whether this inhaler might cause difficulty is to employ it. In my opinion it would be highly unlikely that it would cause any problem.

I hope that I have interpreted your question correctly, and this information is of help to you.

It is also possible that the question you asked is whether or not there was any link between ventilator use and beef surfactant as an infant. I am afraid there is no way to answer that particular question.

Thank you again for your inquiry.

Previous Question and Answer from web site:

11/1/2007 RE: Can lactose allergy cause adverse reactions to inhalers

Question:

I recently prescribed a Pulmicort Flexhaler to a 5-year-old with persistent asthma and milk allergy.

The milk allergy has improved to the point that he recently tolerated a baked good that had milk on the label, yet he experienced facial hives when he ingested yogurt. His mother contacted me and reported that she found on a chat group that the Pulmicort Flexhaler contains lactose whereas the Pulmicort Turbuhaler does not. The child used the Flexhaler for a dose without problem, but she inquired about the safety because of his persistent milk allergy.

I looked at the Flexhaler package insert and did not see lactose listed as an ingredient. It does say that hypersensitivity to any component of the inhaler is a contraindication.

I have seen a report of problems from lactose in Advair in a milk-sensitive asthmatic (JACI 2004), but I cannot find much on lactose and Pulmicort.

I have discontinued the Pulmicort and prescribed a Flovent HFA inhaler. Should all dry powdered inhalers be avoided in milk-allergic individuals?

Answer:

I find it difficult to believe that lactose itself is an allergen. Therefore I doubt (especially since the child has tolerated one treatment) the lactose would be a problem. However, there are at least two troublesome reports in the literature, one of which you have mentioned, and the other of which is cited below, which give me some reservations in this regard.

First, the reasons that I doubt lactose is an allergen:

The major food allergens that are responsible for immediate hypersensitive reactions are soluble glycoproteins. They all have molecular weights from 10 to 70 kD. For a sugar to be antigenic in this regard would be highly unusual. In addition, the major allergens in cow's milk are products of casein and whey. They are therefore either lactoglobulins, lactalbumins, albumins, or various casein molecules. To my knowledge, lactose has never been identified as an allergen in milk. Thus my initial response to you would be that the lactose would not cause this child a problem. However, as mentioned above, there are two disturbing reports that present a caveat regarding this answer. You cited one, and I will give you the reference for a more recent report confirming the one you mentioned.

It is: Morisset, et al. Allergy to cow milk proteins contaminating lactose, common excipient of dry powder inhalers for asthma. J Allergy Clin Immunol 2006; 117(2)(S1):S331-S398 (abstract 369)."

This abstract is a little confusing in that the title states that it is not the lactose, but rather contaminating proteins, and yet an oral as well as a bronchial challenge to lactose was positive. Elimination of lactose was claimed to produce a "clear improvement of eczema and asthma." Thus, in summary, I have doubts regarding any allergenic property of lactose itself, but there are two published reports which give me worry. In one of these, it seems to be suggested that the lactose may be a simple marker for milk proteins.

Unfortunately, I do not know where the lactose is derived (is it milk-extracted?) in this preparation.

Of course, the easiest way to "get around" this problem (which must be extremely rare since there are only two case reports to my knowledge) would be to switch to an aerosol delivered preparation using a spacer, or the Respules.

That is my best answer to a question which may not be completely answerable. I am going to "farm out" your question to see if there is a more expert or dissenting opinion, and when I receive the answer, I will get back with you again.

Follow-up answer from Dr. Sicherer:

For many years we had advised patients that "pharmaceutical grade" lactose was devoid of milk proteins. In retrospect, perhaps no one was looking because patients had not been reporting reactions. However, occasional reactions have been noted, for example in a severely milk-allergic asthmatic patient of the late Gail Shapiro, MD who used a dry powder inhaler containing lactose. Testing of various lactose-containing DPIs (Nowak-Węgrzyn et al JACI 2004) indeed disclosed presence of trace quantities of milk protein. The exact amount was not determined, but there is a notion that lot to lot variability exists. Additionally, the amount of lactose delivered varies by device (e.g., some routinely deliver more of the lactose carrier per inhalation). The package inserts of the DPIs are now typically commenting upon their containing milk protein (associated with the lactose carrier). The product insert I viewed online for the type mentioned here (Flexhaler) did mention milk protein in a parenthetical statement associated with "lactose". Of note, the allergic response would be directed to residual milk proteins (the lactose is derived from skim milk) and not to the milk sugar itself.

As with any food allergy, individuals may have a particular reaction threshold (for example, not everyone reacts to trace amounts). It is probably the case that the trace amount in the inhaler would not trigger a noticeable reaction for most with a milk allergy. However, it has been hypothesized that inhalation of a trace amount may be more likely to cause some reaction (e.g., the respiratory mucosal route having a more direct response and leading to asthma reactions) than if the same amount were eaten (affected by digestion).

We do not have a strong understanding of the extent of contamination in various lactose containing products. There is a study of a lactose containing soy formula where no milk-allergic children reacted and the investigators could not detect residual milk proteins (Fiocchi et al Pediatrics 2003).

As an aside, about 75% of children like the one described here tolerate a small amount of milk baked into a bakery product (e.g., cookies) even though they do not tolerate whole milk proteins (e.g., cheese, milk, yogurt) presumably because the bakery product has less protein and the heating in a airy environment further alters the allergens. Unfortunately, there is no easy way to know who may have this level of tolerance (no accurate skin or serum tests) and we have seen children have anaphylaxis to milk in baked goods.

Though this child described may qualify as one unlikely to react to the trace (if any) residual milk protein in the DPI (basing this assumption on the observation that he tolerated milk in baked goods), and certainly risk/benefit plays a part in decision-making, it seems reasonable to use an equally effective treatment without this additional concern. I am not aware of a DPI that has lactose and has been proven NOT to have potential milk contamination.

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From Allergy and Asthma News:

Allergy/Asthma Information Association  
Milk Proteins and Allergy Medications

Dr. Antony Ham Pong of Ottawa has compiled some information on milk allergy and asthma/allergy medications that have trace amounts of cow's milk protein. He recommends that his patients who have cow's milk allergy not use dry powder inhalers (DPIs) with lactose because of the risk of inhaling trace amounts of milk protein causing a severe asthma attack. There are alternatives which are lactose free. "Inhaling a trace amount of milk protein is likely far more dangerous to a milk allergic asthmatic person than ingesting the same trace amount."

With respect to milk allergy and oral meds containing lactose, the risk is far lower because the trace amounts are unlikely to cause allergic reactions except in the most severely allergic cases. Therefore, only in cases of severe milk anaphylaxis does he recommend avoiding

lactose containing oral meds. However, the specific advice is up to the allergist in a specific case.

#### Cow's milk Allergy & Lactose - Containing Medications

Pharmaceutical grade lactose contains trace amounts of milk protein (0.012 - 0.029% N impurities including cow's milk).

These trace amounts can cause allergic reactions in severely milk allergic individuals if ingested or inhaled.

There are two case reports of allergic reactions to inhaled asthma meds containing lactose, one severe in a child, the other in an adult.

Advair diskus monograph now states "contraindicated in patients with IgE-mediated allergic reactions to lactose or milk".

Cow's milk allergy usually remits by age 2-3 years, but could be lifelong

#### Lactose Containing Asthma/Allergy Meds

- Singulair 4 mg granules & 10 mg tabs (but not 4 & 5 mg tabs)
- Reactine, Alerius, Claritin tabs (but not liquid forms). Allegra is lactose free
- Benadryl 50 mg pink/white capsule (not caplet, chewable tabs or liquid)
- Prednisone tabs but not Pediapred

#### Lactose Containing Asthma Inhalers

Lactose containing dry powder inhalers

Advair diskus

Flovent diskus

Foradil aerolizer capsules

Oxeze turbuhaler

Spiriva capsules

Symbicort turbuhaler

Ventolin diskhaler, diskus, rotacaps

#### Lactose-Free DPIs

Bricanyl

Pulmicort

All pressurized spray asthma inhalers (MDIs) are lactose free.

#### Lactose Intolerance & Asthma Meds

- Lactose intolerance symptoms can occur if multiple lactose containing meds are ingested

Lactose in DPIs is not likely an issue e.g., Advair discus contains 12.5 mg lactose but 3,000 mg are needed to provoke symptoms - the equivalent to amount found in 60 ml milk or 180 gm processed cheese.

Sincerely,

Phil Lieberman, M.D.

Key Words: lactose, milk allergy, asthma inhalers, milk proteins

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